REMARKS

STATUS OF THE CLAIMS

Claims 1-7 and 10-31 are pending, as shown above. By amendment herein, claim 11 has been amended to make explicit what was previously implicit, namely to specify that the sequence encoding the viral immunogen carried by the plasmid is operably linked to a promoter that is the only promoter sequence on the plasmid and that the chemokine is administered as a polynucleotide. It is to be understood that the plasmid may further include additional control sequences, for example enhancers and the like. Support for the amendment is found throughout the specification as filed, for example on page 7, lines 17 and 21 as well as Table I on page 9. Claims 12-15 have been canceled, without prejudice or disclaimer. New claim 32 has been added and is directed to embodiments, in which only the chemokine and plasmid are administered, as disclosed in the Examples.

PRIORITY

The Office Action states that Applicant is not entitled to the priority date of the provisional application. (Office Action, pages 2-3). In particular, it is alleged that the cited provisional application did not disclose B lymphocyte chemoattractant. (Office Action, page 3).

Applicant submits that various references cited in the provisional application and incorporated by reference into the utility application sufficiently describe B lymphocyte chemoattractant in such a way that one of skill in the art would have recognized that Applicant was in possession of the claimed invention at the time the provisional was filed. The provisional application discloses that administration of a polynucleotide encoding a chemokine induces "migration of antigen presenting cells and/or lymphocytes to the site of administration." *See,* page 3, lines 22-25 of the U.S. Serial No. 60/082,600. Reference no. 22 in both the provisional and utility (Butcher et al.) also discusses trafficking of lymphocytes, including B lymphocytes. Thus, Applicant is entitled to the priority date of the provisional application.

35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION/NEW MATTER

Claims 11-29 stand rejected under 35 U.S.C. § 112, first paragraph. (Office Action, pages 3-4). In particular, it is maintained that the original disclosure fails to specify subject matter regarding "a single control sequence derived from a virus" as claimed. (Office Action, page 3). In support of this new matter rejection, selected portions of M.P.E.P. § 2163.02 are cited in the Office Action. (Office Action, page 4).

Applicant submits that the foregoing amendment to claim 11 obviates this rejection. To the extent that any objections remain to the recitation "single promoter derived from a virus," Applicant traverses the rejection and supporting remarks because the as-filed specification clearly describes the subject matter of claims 11-29.

It is well settled that the proscription against the introduction of new matter in a patent application (35 U.S.C. 132 and 251) serves to prevent an applicant from adding information that goes beyond the subject matter originally filed. See, *e.g., In re Rasmussen*, 650 F.2d 1212, 1214, 211 USPQ 323, 326 (CCPA 1981) and MPEP § 2163.06. The Office Action implies that literal support is required, when, in fact, relevant portions of M.P.E.P. § 2163.02 omitted from the Office Action, specifically indicate the reverse, namely:

> The subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement.

Thus, the written description requirement is satisfied if the specification reasonably conveys possession of the invention to one skilled in the art. *See, e.g., In re Lukach,* 169 USPQ 795, 796 (CCPA 1971). The disclosure must be read in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange,* 209 USPQ 288 (CCPA 1981). Moreover, the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976).

In the pending case, the as-filed specification clearly conveys that Applicant was in possession of plasmids including a single promoter derived from a virus. Throughout the Examples, Applicant indicates that expression of the viral immunogen is controlled by elements derived from a cytomegalovirus (CMV), for instance:

> Each plasmid comprises a CMV enhancer/promoter and is Kanamycin-resistant. (page 7, lines 17-18).
>
> Plasmid pCMVKmΔNS comprises hepatitis C viral DNA.... (page 7, line 21).

Therefore, a skilled artisan would have plainly recognized that that Applicant was in possession of the claims single promoter plasmids. CMV is clearly a virus and the use of CMV promoters was common at the time of filing.

In view of these facts and the failure of the Office to provide evidence as to why the skilled artisan would not have understood that Applicant was in possession of the subject matter of claims 11-29, withdrawal of this rejection is respectfully requested.

35 U.S.C. § 112, SECOND PARAGRAPH

Claims 11-29 were rejected as allegedly indefinite for reciting "a single control sequence derived from a virus." (Office Action, page 5).

Without conceding the correctness of the Examiner's position and solely to expedite prosecution by making explicit what was previously implicit, Applicant has amended independent claim 11 to recite "a single promoter." The term is clearly used in the specification to refer to a plasmid that contains only one promoter. *See, e.g.,* page 7, line 17. Thus, Applicant respectfully requests withdrawal of this rejection.

35 U.S.C. § 102(E)

Claims 1, 2, 5-7, 10-22, and 25-31 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,569,418 (hereinafter "Garzino-Demo"). (Office Action, page 6).

Garzino-Demo is not a proper reference under 35 U.S.C. § 102(e). Applicant notes that Garzino-Demo purports to the claim the benefit of a PCT application filed December 11, 1998 (US98/26291) and provisional application filed December 11, 1997. However, Applicants note that the disclosure in Garzino-Demo relied upon by the Examiner in making this rejection (namely, Fig. 3B, col. 7, lines 33-50 discussing BLC) does not appear to be present in the PCT application. Thus, at best, the cited disclosure in Garzino-Demo regarding BLC was first disclosed in March 2, 2000. Since both Applicant's provisional and PCT applications pre-date Garzino-Demo's apparent priority date, the rejection under 35 U.S.C. § 102(e) cannot be sustained and withdrawal thereof is respectfully requested. Should the Examiner maintain the rejection, Applicant requests that the disclosure relied upon by the Examiner in the priority document be pointed out with particularity.

35 U.S.C. § 103

A. Rejection Based on Garzino-Demo

Claims 1, 3, 4, 11, 23 and 24 stand rejected under 35 U.S.C. § 103 as allegedly unpatentable over Garzino-Demo in view of U.S. Patent No. 6,297,048 (hereinafter "Jolly"). (Office Action, page 7).

For the reasons noted above, Applicant submits Garzino-Demo cannot be used as a reference against the pending claims, alone or in combination with any other reference. Accordingly, the obviousness rejection based on Garzino-Demo should be withdrawn.

B. Rejection Based on Hurwitz

Claims 11-13, 16, 17, 21, 25 and 27-29 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 5,846,546 (hereinafter "Hurwitz"). (Office Action, page 8). In support of this rejection it is stated:

> Hurwitz et al teach an immunogenic composition comprising a bi-functional plasmid vector encoding HIV envelope protein-coding region (abstract), and further comprising a polynucleotide encoding a chemokine such as MIP1α (2nd paragraph, column 29). ... The bi-functional viral vector comprises one promoter (CMV, viral derived control sequence as used by the instant applicants) for expression in mammalian cells, and another promoter for preparation of viral vector (column 4, lines 41-45). ...
>
> The claimed invention is obvious over Hurwitz et al because Hurwitz et al clearly teach they are providing a new plasmid, wherein only one promoter is required for expressing the antigen-chemokine protein in mammalian cells (column 4, lines 41-45). (Office Action, pages 7-9).

The Examiner's rejection is legally and factually inaccurate.

Legally, in order to establish a *prima facie* showing of obviousness, the onus remains on the Office to point to teachings or suggestions within the references themselves that would lead one of skill in the art to combine them as cited. *See, e.g., In re Rijckaert,* 28 USPQ2d 1955, 1957 (Fed. Cir. 1993), emphasis added. The Office cannot simply state, as it has done in this case, that teaching the advantage of a "bi-functional plasmids" is tantamount to suggesting the use of single promoter plasmids, as claimed. Here, there is nothing in Hurwitz that would lead one to the methods as claimed.

Factually, the Office Action has clearly misinterpreted many of Hurwitz's teachings. In particular, Applicant notes that the Examiner errs in asserting that Hurwitz teaches or suggests polynucleotides encoding MIP1α. *See,* Office Action, page 8, citing col. 29 of Hurwitz. In point

of fact, it is clear from Hurwitz's disclosure in the second paragraph of column 29 that the use of MIP1α is contemplated only when used as a protein. The referenced passage is silent as to polynucleotides and, indeed, recites a laundry list of "antiviral chemotherapeutic compounds" including a variety of proteins and non-protein chemicals. That being the case, Applicant queries how would one administer the various molecules (including non-proteins) at column 29 of Hurwitz as polynucleotides. Certainly, there is no teaching in Hurwitz suggesting that MIP1α (or any of the other proteins disclosed at column 29) could be administered as polynucleotides. Thus, pending claims 11, 16, 17, 21, 25 and 27-29, directed to methods in which the chemokine is administered as a polynucleotide, are not obvious over Hurwitz.

In addition, Applicants disagree with the assertion that Hurwitz somehow suggests using single-promoter plasmids encoding a viral immunogen in combination with a chemokine and in the absence of additional immunogenic compositions. *See,* new claim 32, directed to methods "consisting of" administering a plasmid and chemokine in any order. In fact, the polyenv compositions of Hurwitz are provided in viral vectors. Hence, Hurwitz notes that it was necessary to develop a new multiple-promoter plasmid, because of the need to provide recombinant viral vectors:

> The foregoing methods of the invention provide the incentive to genetically engineer a new plasmid vector. Thus, in corollary aspect, the present invention provides a bi-functional plasmid that can serve as a DNA vaccine and a recombinant virus vector, comprising a heterologous insertion site under control of both an animal expression control sequence and a viral expression control sequence. Preferably, the animal expression control sequence is a cytomegalovirus immediate early (CMV) promoter, and the virus expression control sequence is a vaccinia virus early promoter, a vaccinia virus late promoter or both. (col. 4, lines 41-51).

Simply put, Hurwitz does not teach or suggest the use of single promoter plasmids, as claimed.

The steps of the claimed methods, including the use of single-promoter plasmids, are precisely defined in the claims themselves, not in Hurwitz or the state of the field generally. To assert that Hurwitz (or the art) somehow teaches the use of single promoter plasmids as claimed, involves, at the very least, improper hindsight reconstruction. There is nothing in Hurwitz that would lead a skilled artisan to the conclusion that single promoter plasmids in combination with chemokines would function as claimed. Thus, Hurwitz does not teach or suggest any of the claimed methods.

C. Rejection Based on Hurwitz and DeVico

Claims 11-21 and 23-29 stand rejected as allegedly obvious over Hurwitz in view of U.S. Patent No. 6,214,540 (hereinafter "DeVico"). (Office Action, page 10). Hurwitz is cited as above. DeVico is cited for teaching the use of chemokines for HIV therapy using chemokines.

There is no combination of Hurwitz and DeVico that renders the pending claims obvious. Nowhere do Hurwitz or DeVico describe or suggest methods using single-promoter plasmids to generate an immune response; methods in which a plasmid encoding an immunogen and BLC are administered; or methods in which a chemokine (or polynucleotide encoding a chemokine) and plasmid encoding an immunogen are administered successively in either order. Indeed, as noted above, Hurwitz fails to suggest the use of plasmids having a single (virally derived) promoter sequence that drives expression of immunogen. Thus combining Hurwitz with DeVico would result, at best, in a bifunctional plasmid that includes sequences encoding either an immunogen derived from a chemokine (DeVico). In contrast, the pending claims clearly teaches that, when the chemokine is encoded by a polynucleotide it is carried on a plasmid separate from the one carrying the sequence encoding the viral immunogen.

In sum, there is no motivation in either Hurwitz or DeVico to generate an immune response by administering, as separate molecules, a single-promoter plasmid and a chemokine. Thus, the methods as claimed are not obvious over any combination of Hurwitz and DeVico and withdrawal of this rejection is requested.

D. Rejection Based on Chandrashekar

Claims 11-13, 16, 17, 21, 27, and 29 stand rejected as allegedly obvious over U.S. Patent No. 6,383,774 (hereinafter "Chandrashekar") in view of Hurwitz. (Office Action, page 10). and Chandrashekar is cited for teaching plasmids containing immunogens derived from parasites.

For the reasons of record and those reiterated herein, Applicants traverse the rejection and supporting remarks.

There is no teaching or suggestion in Chandrashekar regarding methods of enhancing an immune response to a viral immunogen by administering a single-promoter plasmid encoding the viral immunogen and a chemokine (or polynucleotide encoding a chemokine). Chandrashekar contains no disclosure regarding viral immunogens. Nonetheless, the Office has repeatedly asserted that this reference teaches, citing column 26, that chemokines enhance the response to "any" antigen. In reality, column 26 of Chandrashekar defines an adjuvant as agents that "are capable of enhancing the immune response of animal to a specific antigen." This is a far cry from teaching that the all the listed antigens work equally well with <u>any</u> antigen. Thus, the fact

remains that Chandrashekar teaches nothing about viral antigens and whether or not chemokines "are capable of," let alone actually do, enhancing the immune response to a viral immunogen, as claimed.

For its part, for the reasons of record and detailed above, Hurwitz fails to teach or suggest methods in which a single-promoter plasmid encoding a viral immunogen is administered with a chemokine.

Accordingly, because there is no teaching or suggestion within the references to arrive at any of the claimed subject matter, withdrawal of the rejections is respectfully requested.

CONCLUSION

For the reasons state above, Applicant respectfully submits that the pending claims define an invention that is novel, non-obvious, fully enabled and described by the specification. Accordingly, Applicant requests that the rejection of the claims be withdrawn, and that the application proceed to allowance.

Please direct all further communications regarding this application to:

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